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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/862,855	05/21/2001	Hong Cai	S-94,652	8369

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/862,855	CAI ET AL.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *5,17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-16,18,19 and 21* is/are rejected.

7)☒ Claim(s) *6,7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed October 16, 2006. Claims 1-21 were previously pending, with claims 5, 17 and 20 withdrawn from consideration. Applicants amended claims 2, 4 and 21. Claims 1-21 are pending, with claims 5, 17 and 20 withdrawn from consideration.

2. The declaration filed on October 16, 2006 under 37 CFR 1.131 is sufficient to overcome the Landers reference (U.S. Patent No. 6,844,154 B2). Consequently, the following rejections are withdrawn: the rejection of claims 1-4, 8-16, 18 and 19 under 35 U.S.C. 102(e) as anticipated by Landers and the rejection of claims 6, 7 and 21 under 35 U.S.C. 103(a) over Landers and Nie et al.

3. All other previously presented rejections are maintained for reasons given in the "Response to Arguments" section below.

4. This office action is made non-final because of new grounds for rejection.

Response to Arguments

5. Applicant's arguments filed October 16, 2006 have been fully considered but they are not persuasive.

Regarding the rejection of claims 2, 8-16, 18 and 19 under 35 U.S.C. 102(b) as anticipated by Chehab et al., Applicants argue the following:

A) The claimed method does not require target amplification or detection of amplified DNA, but is drawn to detection of fluorescent probes bound to unamplified target fragments.

B) The claimed invention is based on single-molecule detection, and the limitations of illuminating each labeled DNA or RNA segment with light beam and detecting the presence or absence of each luminescent probe on each segment are not disclosed or suggested by Chehab et al., who teach visualization of amplified DNA, not probes.

C) The approach of Chehab et al. cannot be used to detect SNPs separated by more than several thousand base pairs.

Regarding A), there is nothing in claim 2 or the dependent claims that restricts the method to detection of unamplified fragments, as the preamble reads "comprising the steps of", thus permitting additional steps in addition to the ones claimed.

Regarding B), there are no limitations of detecting single molecules in the claims. In addition, Chehab et al. specifically teach detection of DNA fragments with fluorescent probes (page 9179, third paragraph, for example). Further, since the amplified fragments with probes bound to them are illuminated with the light and detected, Chehab et al. inherently teach detection of each of the segments.

C) This argument is drawn to a feature which is not a claim limitation.

The rejection is maintained.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 2, 8-16, 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Chehab et al. (PNAS USA, vol. 86, pp. 9178-9182, 1989).

Regarding claim 2, Chehab et al. teach a method of rapid haplotyping, the method comprising:

labeling at least two target sites on a segment of DNA or RNA with separate distinguishable luminescent hybridization probes, where the targets are selected genetic markers (Chehab et al.

teach differential labeling oligonucleotide primers specific for target sites on the β-globin gene, the target sites being a 4-bp deletion at codons 41/42 and a C to T substitution at IVS1 and annealing the primers to genomic DNA, therefore labeling the two sites with distinguishable hybridization probes (page 9178, last two paragraphs; page 9179, paragraphs 1-3).);

forming a dilute solution containing the labeled DNA or RNA segments (Chehab et al. teach forming dilute solutions of amplified labeled fragments (page 9179, second paragraph).);

illuminating each labeled DNA or RNA segment with light beams (Chehab et al. teach illuminating the tubes with amplification reactions using light beams (page 9179, second and third paragraph).); and

detecting the presence or absence of each luminescent hybridization probe on each DNA segment to determine the haplotype of each DNA or RNA segment (Chehab et al. teach detection of the presence of hybridization probes and determination of the haplotype of each segment (page 9179, paragraphs 3-5; page 9181, second paragraph; Table 1).).

Regarding claim 8, Chehab et al. teach single nucleotide polymorphism and multibase deletion (page 9178, fifth paragraph).

Regarding claims 9 and 12, Chehab et al. teach the primers having distinguishable colors (=luminescence emission spectral distribution) (page 9178, last paragraph; page 9179, first paragraph).

Regarding claims 10 and 13, Chehab et al. teach single dye molecules (page 9178, last paragraph; page 9179, first paragraph).

Regarding claims 11, 14, 16 and 19, Chehab et al. teach DNA probes (page 9178, last paragraph).

Regarding claims 15 and 18, Chehab et al. teach single probes specific for each target (page 9179, third paragraph).

8. Claims 1, 3, 4, 9-11, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kostrikis et al. (Science, vol. 279, pp. 1228-1229, 1998; cited in the IDS).

Regarding claim 1, Kostrikis et al. teach a method for characterizing a genetic profile of a chromosome pair, the method comprising:

forming multiple luminescent hybridization probes to hybridize to a wild-type and a mutant polymorphism at a first polymorphic target site and to a wild-type and a mutant polymorphism at a second polymorphic target site, where the probes for the wild-type polymorphic sites have at least one recognizable luminescent characteristic and the probes for the mutant polymorphic sites have at least a second recognizable luminescent characteristic and where the first and second polymorphic sites are located on the selected chromosome and are linked to a selected genetic characteristic (Kostrikis et al. teach forming at least two luminescent pairs of probes for at least two polymorphic sites, where each pair contains a probe hybridizing to a wild-type polymorphism and a probe hybridizing to a mutant polymorphism, and where each probe is labeled with a different fluorescent label (Fig. 1; page 1228, second and third paragraph).);

forming single stranded DNA at least along segments of DNA forming the chromosome, where the single stranded DNA segments contain the first and second polymorphic sites (Kostrikis et al. teach forming single stranded DNAs along fragments of genomic DNA containing the polymorphic sites (Fig. 1; page 1228, paragraphs 3-5; page 1229, first paragraph). Since the amplification reaction requires denaturation of double-stranded DNA to form single strands, Kostrikis et al. inherently teach formation of single-stranded DNA).);

forming probe pairs from the luminescent probes, where each probe pair contains a probe specific to the first polymorphic site and a probe specific to the second polymorphic site (Kostrikis et al. teach forming at least two luminescent pairs of probes for at least two polymorphic sites, where each pair contains a probe hybridizing to a wild-type polymorphism and a probe hybridizing to a mutant polymorphism, and where each probe is labeled with a different fluorescent label (Fig. 1; page 1228, second and third paragraph).);

specifically hybridizing each probe pair in separate solutions of the single stranded DNA and determining the presence or absence of each luminescent hybridization probe in each segment of DNA in each solution to obtain a set of outputs (Kostrikis et al. teach specifically hybridizing each probe pair in separate solutions of the DNA and determining the presence or absence of each hybridization probe (page 1228, paragraphs 2-5; page 1229, first paragraph).); and

analyzing the set of outputs from the hybridized probes to determine the complete haplotype that characterizes the genetic profile of the selected chromosome pair (Kostrikis et al. teach analyzing the set of outputs to determine the haplotype of the chromosome pair (Fig. 1, 2; page 1229, second paragraph).).

Regarding claim 3, Kostrikis et al. teach genotyping other alleles (page 1229, third paragraph).

Regarding claim 4, Kostrikis et al. teach detecting a signal emitted by each probe (Fig. 1; page 1228, second paragraph).

Regarding claim 9, Kostrikis et al. teach detection of the probes based on their emission spectral distribution (page 1228, second paragraph).

Regarding claim 10, Kostrikis et al. teach molecular beacons (page 1228, second paragraph).

Regarding claims 11 and 16, Kostrikis et al. teach DNA probes (page 1229, reference 12).

Regarding claim 15, Kostrikis et al. teach single probes specific for each target (page 1228, second paragraph; page 1229, reference 12).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kostrikis et al. (Science, vol. 279, pp. 1228-1229, 1998; cited in the IDS).

A) Teachings of Kostrikis et al. are presented above. They do not specifically teach forming dilute solutions of DNA fragments, but teach application of the method to direct target detection without amplification (page 1229, last paragraph).

Therefore an ordinary practitioner would have recognized that the optimizable variable of DNA segment concentration could be adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of specific times for amplification was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

11. No references were found teaching or suggested claims 6 and 7. Claims 6 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
12/21/06